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16. ABSTRACT

Respiratory functions were measured daily by spirometry over four weeks at a summer camp in northwestern New Jersey. Multiple regression analyses indicated that O_3 concentration, cumulative daily O_3 exposure, ambient temperature, and humidity were the most explanatory environmental variables for daily variations in function, and that O_3 concentration had, by far, the strongest influence on FVC, PEFR, and MMEf. For FEV_1, cumulative daily O_3 exposure and heat stress had greater relative effects. Linear regressions were performed for each child between O_3 concentration and function, and all average slopes were significantly negative ($p < 0.05$) for FVC, FEV_1, PEFR and MMEF for all children, and for boys and girls separately. The implications of these short-term effects are unknown. However, the results in these free living children are comparable to those found in chamber studies with comparable exposures.

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Effects of Ambient Ozone on Respiratory Function in Active, Normal Children[1-3]

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SUMMARY Respiratory functions were measured on a daily basis by spirometry over a period of 4 wk at a summer camp at Fairview Lake in northwestern New Jersey. Fifty-three boys and 38 girls 8 to 15 yr of age participated in the study on at least 7 days; 37 children were in residence for 4 wk, 34 for the first 2 wk only; and 20 for the last 2 wk. There were 72 whites, 15 blacks, 3 Asians, and 1 Hispanic in the study group.

Multiple regression analyses indicated that the O_3 concentration in the previous hour, the cumulative daily O_3 exposure during the hours between 9 A.M. and the function measurement, ambient temperature, and humidity were the most explanatory environmental variables for daily variations in function, with the 1 - h O_3 concentration having the strongest influence. Linear regressions were performed for each child between O_3 concentration and function, and all average slopes were significantly negative ($p < 0.05$) for FVC, FEV_1, PEFR, and FEF_{25-75} for all children, and for boys and girls separately. Comparable results were obtained in data subsets (i.e., children studied during the first or second 2 wk only, and for data sets truncated at $O_3 < 80$ and $O_3 < 60$ ppb). The average regression slopes (± SE) for FVC and FEV_1, respectively, were -1.03 ± 0.24 and -1.42 ± 0.17 ml/ppb, whereas for PEFR and FEF_{25-75} they were -6.78 ± 0.73 and -2.46 ± 0.26 ml/s/ppb. These predict average decrements of 4.9, 7.7, 17, and 11%, respectively, for O_3 at the current ambient standard of 120 ppb. The implications of these short-term effects are unknown. However, the results in these free-living children are comparable to those found in chamber studies with comparable exposures.

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Introduction

A pilot study of the effects of ambient exposures to summertime hazy air on respiratory function in children was performed in 1980 in Indiana, PA. We found significant O_3-related decrements in respiratory function even though the highest 1-h maximal O_3 was only 110 ppb, a concentration below the current National Ambient Air Quality Standard (NAAQS) of 120 ppb for 1 h.

Specifically, spirometry was done on 58 summer camp children over several weeks. The results of that study showed that ambient exposure of active children produced an average decrement in FVC of 1.06 ml/ppb, and an average decrement of 0.78 ml/ppb in FEV_1 (1). For mini-Wright peak flow for 23 children measured on each of 8 days, the average decrement per ppb of O_3 was 2.62 ml/s/ppb. For 33 other children measured on 6 camp days, the decrement did not reach statistical significance, but the average was 1.77 ml/s/ppb, which was consistent with that of the group measured on 8 occasions (2). In a follow-up pilot study on a group of 39 less active children in Mendham, NJ, in 1982, we found smaller and nonsignificant decrements in FVC and FEV_1, but highly significant changes in peak expiratory flow rate (PEFR) from the spirometric tracings (2, 3). We also found that after a haze episode in which the O_3 exposures exceeded the NAAQS for 4 consecutive days, including a maximal 1-h exposure of 185 ppb, there was a baseline shift in PEFR lasting approximately 1 wk (3).

In another epidemiologic field study, Lebowitz and coworkers (4) measured young children and adolescents with the mini-Wright peak flow meter and found that PEFR declined with both ozone and total suspended particulate (TSP) matter.

In a chamber exposure study by McDonnell and coworkers (5), twenty-two 8- to 11-yr-old boys were exposed at 1-wk intervals to either pure air or 120 ppb O_3 during heavy intermittent exercise ($\dot{V}_E$ = 38 L/min). The average change in FEV_1 after air exposure was −10 ml, whereas after O_3 it was −67 ml. The difference of −57 ml corresponds to 0.48 ml/ppb, a value intermediate to those seen in the Indiana, PA, and Mendham, NJ, studies.

In a study on 59 healthy adolescents 12 to 15 yr of age, Avol and associates (6, 7) measured the pulmonary function on 2 occasions, 3 wk apart, in a mobile laboratory. On one occasion, the subjects were exposed for 1 h during continuous exercise ($\dot{V}_E$ = 32 L/min) to either ambient air containing 150 ± 4 ppb O_3 and 153 ± 30 µg/m³ TSP matter, or to purified air. Although no information was provided on the size distribution or composition of the TSP matter, the aerosol in the region generally is a mixture of fine particle nitrate, sulfate, and photochemically generated organic matter, plus coarse particle soil and road dust. The average change in FEV_1 after purified air exposure was −0.49%, whereas after the ambient air exposure it was −4.20%. For the average pre-exposure FEV_1 of 2,855 ml, the 120-ml drop in FEV_1 represents a decline of 0.80 ml/ppb.

In this study, our objective was to more definitively establish the effects of ambient exposure to ozone on the respira-

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[3] The research described in this report has been reviewed by the Health Effects Research Laboratory of the Environmental Protection Agency and approved for publication. Approval does not signify that the contents necessarily reflect the views of the agency.

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tory functions of active children, and to investigate the influence of other air pollutants and environmental factors on the apparent responses to ozone. The study was performed during the summer of 1984 at a YMCA camp at Fairview Lake in northwestern New Jersey on 91 children in residence at the camp for either 2 or 4 wk. As in our previous summer studies on children, the location was remote from strong local sources of air pollution and within the region of the northeastern United States which is periodically exposed to hazy air masses enriched in O_3 and sulfate aerosols.

Unlike our previous summer studies on children in day camp programs, the children in this study were in residence at the camp and available for respiratory function measurements every day. Their sleeping shelters had screens, but were otherwise not fully enclosed, so that they were exposed to the measured ambient air concentrations throughout the study. This permitted better characterization of their cumulative daily exposures than was possible in the previous camp studies. Finally, on the basis of the scheduled activities in each camp, and our direct observations, the level of physical activity during the day at Fairview Lake was comparable to that observed at Indiana, PA, in 1980, and substantially greater than that observed at our 1982 study in Mendham, NJ.

Methods

The study design and methodology have been described in detail elsewhere (8). The following is a brief description of the most important features of the experimental protocol and methods.

Ninety-one children (53 boys and 38 girls) 8 to 15 yr of age participated in the study and had validated spirometric data on at least 7 days; 37 of these children remained in camp for 4 wk, 34 for the first 2 wk only, and 20 for the last 2 wk of the study. Their homes were mainly in eastern New Jersey and other locations in the Metropolitan New York region. The ethnic composition of the groups was 72 white, 15 blacks, 3 Asians, and 1 Hispanic. For each child, an informed consent was obtained from either a parent or a guardian who completed a standardized questionnaire on the child's medical history. None of the children had any history of lung disease or atopy, and they were all nonsmokers. There were no reports of respiratory illness in the week preceding the start of the study or during their participation in the study. At some point during the study, each child was measured for height and weight in stocking feet.

Measurements of pulmonary function were made on almost all of the children on every day of their stay in camp. This was done inside a mobile laboratory that housed all equipment and was located within a one-quarter mile radius of most camp activities. The measurements were performed between 11:30 A.M. and 6:30 P.M., during breaks in the programmed activities of the children or in their free periods. There was no attempt to measure the children at the same time of day on each day. It was considered more important to accommodate the camp schedules and children's availability in order to achieve the highest possible participation on each day.

On each daily visit to the mobile laboratory, the children underwent 3 types of examinations: (*1*) they answered a simple symptoms questionnaire to see if they had any hoarseness, sore throat, cough, phlegm, chest pains, wheeze, runny or stuffy nose, or eye irritations; (*2*) their peak expiratory flow was then measured, using a mini-Wright peak flow meter, and 3 values were recorded, (*3*) they performed spirometry tests on an 8-L Collins portable recording spirometer (Warren E. Collins, Braintree, MA) in a sitting position with a noseclip. Two identical spirometers were used for simultaneous measurements on individual children, and the assignment of each child on each day to a spirometer was at random. Each spirometer volume was calibrated daily using a standard 3-L syringe. Atmospheric pressure, room temperature, and time of day were recorded for each test. The spirometry test consisted of a minimum of 3 acceptable forced maximal expiratory maneuvers yielding volume-time tracings. Neither the staff administering the spirometry nor the children were informed of the concentrations of the pollutants. The acceptance criteria were that: (*1*) the 3 best FVC values should not vary by more than 200 ml, (*2*) the curve rise time should be smooth and start from at most 200 ml, (*3*) the entire curve should have no bumps or dips, (*4*) the curve must last for at least 4 s, and (*5*) the curve must reach a plateau that lasts at least 1 s. From the 3 best tracings made by each child in a day, the following parameters were determined according to the criteria established by the ATS Snowbird Workshop (9): FVC, FEV_1, FEF_{25-75}, and PEFR. All parameters were standardized to BTPS.

Each tracing was read by 2 independent observers, and the results were stored in computer files for further statistical analysis. When the results were discordant by more than 10%, they were reviewed by a third reader.

The data sets were examined for statistical outliers. Outliers were defined as data points lying more than 2 standard deviations from the O_3 versus function regression lines. There were very few points so designated, and these few were only slightly beyond this limit. Accordingly, all data were retained in the analyses.

The mobile laboratory also housed automated direct monitors for pollutant and environmental data collection, and supported an array of filter samplers. Continuous data were collected for ambient temperature, humidity, wind speed and direction, and the concentrations of O_3, H_2SO_4, and total sulfates. O_3 was measured by UV absorbance, and H_2SO_4 and total sulfates were alternately determined by a flame photometric sulfur analyzer (Model 285; Meloy Laboratories, Springfield, VA) preceded by a programmed thermal pretreatment unit (10).

Quality assurance audits for the O_3 monitors were performed at the site by the New Jersey Department of Environmental Protection (NJDEP). Daytime O_3 concentrations at the camp had to be estimated for several brief periods, less than 2% of all sampling hours, when on-site monitoring data were missing. These estimates were based on data collected at the nearby Chester, NJ, site of NJDEP and regression analyses of the coincident daytime Fairview Lake and Chester O_3 concentrations during meteorologically similar days throughout the balance of the period.

The ambient aerosol samples were collected on quartz fiber filters with a dichotomous sampler having a 15-μm fractionating inlet (PM_{15}) and a coarse/fine cut size of 2.5 μm (Sierra Model 244-E; Carmel Valley, CA). Two 4-h samples were taken daily: at approximately 10 A.M. to 2 P.M. and 2 P.M. to 6 P.M. The fine filters were extracted in the field in polycarbonate vials containing 20 ml of 5×10^{-5} M $HClO_4$. These filters were stored in a refrigerator and ultimately sent to and analyzed by Northrup Services, Inc. (Research Triangle Park, NC). Aerosol acidity, as measured by strong acid (H^+) content, was determined using the pH method (11). Sulfate, nitrate, and ammonium content were measured by ion chromatography (12).

Linear regressions were calculated between the functional measures for each child and the average O_3 concentrations in specific time periods (i.e., 1, 2, or 4 h) preceding the measurement of function. For a function measurement made in the first 30 min of an hour, the time period extended from the start of an hour. For a function measurement made in the second 30 min of an hour, the exposure period used extended from the start of a half hour.

Linear regressions also were performed between the functions and day of study, and stepwise multiple regressions were performed with various combinations of environmental variables. The influences of the other candidate environmental variables on the O_3-function regressions were analyzed by examining the average deviation of each point from the regression as a function of each candidate variable.

To explore the relative importance of the environmental variables in the variability in the functional data, we performed a forward-stepwise multiple regression analysis of all the exposure variables considered to be potentially significant. In addition to 1-h O_3, they were: temperature, humidity, H^+ concentration, PM_{15}, number of hours of activity between 9 A.M. and the time of the function measurements, and cumulative daily O_3 exposure. The latter was the sum of the hourly

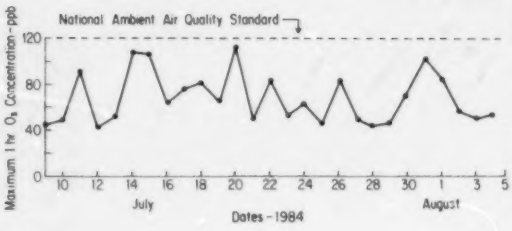


Fig. 1. Maximal 1-h ozone concentrations at Fairview Lake during study period.

O_3 concentrations between 9 A.M. and the time of the function measurements. The basis for the last 2 indices was that camp activities began after breakfast at 9 A.M. Variables were included in the resulting regressions when the F values were < 0.4, and were removed when F was > 0.6. For each child and for every linear single and multiple regression, the coefficients of the fit, values of Student's *t* test and F tests, correlation coefficients (r^2), and residuals were stored.

Results

Exposure Variables

The daily levels of 1-h peak O_3 concentrations are shown in figure 1. It can be seen that the O_3 did not exceed the current NAAQS nor was there any sustained period of O_3 above 100 ppb. The maximal values recorded for H_2SO_4, NH_4HSO_4 and PM_{15} were 4, 20, and 75 $\mu g/m^3$, respectively. Sulfuric acid accounted for a detectable fraction of the total sulfate, i.e., > 2 $\mu g/m^3$, 1-h average, on 5 of the days. Ambient temperatures above 30°C were recorded on only 1 day, with a maximum of 31°C. The only exposure variables that were highly intercorrelated were 1-h O_3 and cumulative daily O_3 (r = 0.72). The correlations between 1-h O_3 and other variables were much lower, i.e., temperature (r = 0.37), humidity (r = 0.25), and H^+ (r = 0.13).

Regressions of Spirometric Measurements with Day of Study

Because repetitive, i.e., virtually daily, measurements of function were being made on each child, it was important to establish whether there was any trend in function with day of study to determine if measured function was improving because of training or diminishing because of loss of motivation. Thus, regressions of FVC, FEV_1, PEFR, and FEF_{25-75} versus day of study were performed on all 91 children with 7 or more valid measurement days. There were no significant associations with day of study. If there had been any trends, it would have indicated either a systematic change in function with time in study, or colinearity with an environmental variable that was affecting a measured function. Because there were no consistent trends for the exposure variables during the study, the lack of trends with time in this study suggests that learning and fatigue were not significant confounding factors.

Regressions of Spirometric Measurements with Hour of Day

Because function measurements were made between 11:30 A.M. and 6:30 P.M., it was important to establish whether there was any diurnal variation in function that could have introduced a systematic bias. Regressions for all 4 functional measures for all 91 children showed no significant associations with hour of the day.

Regressions of Spirometric Measurements with Ambient O_3 Concentrations

The regression analysis used a 1-h O_3 averaging time and the function data from days in which the children were engaged in normal camp activities. The active day data were considered to represent the baseline condition, and excluded data collected during or after periods of rain, since levels of physical activity were much lower during rainy periods or when the ground was wet. There were 1 full day and 2 partial days on which it began to rain in the late afternoon. Data collected on the partial rain days before it started to rain were retained in the baseline data set. The average slopes for each of 4 spirometric indices, i.e., FVC, FEV_1, PEFR, and FEF_{25-75}, and for the ratio FEV_1/FVC, for all 91 children with 7 or more valid measurement days, are shown as baseline in the first line of table 1. The second line in table 1 shows the comparable regression slopes when the rainy day data were included in the data set. The third and fourth lines show the regression slopes for the baseline data set when the averaging times for the O_3 exposures

TABLE 1

AVERAGE REGRESSION SLOPES (± SE) FOR RESPIRATORY FUNCTION INDICES VERSUS AMBIENT OZONE CONCENTRATIONS, NYU-HARVARD-EPA FIELD STUDY AT FAIRVIEW LAKE, NJ, YMCA CAMP: SUMMER 1984

Data Set	Children (*n*)	O_3 Average Time (*h*)	FVC (*ml/ppb O_3*)	FEV_1 (*ml/ppb*)	PEFR (*ml/s/ppb*)	FEF_{25-75} (*ml/s/ppb*)	FEV_1/FVC (*%/ppb*)
Base	91	1	−1.03 ± 0.24*	−1.42 ± 0.17*	−6.78 ± 0.73*	−2.48 ± 0.26*	−0.012 ± 0.006*
Base + RD	91	1	−1.12 ± 0.22*	−1.32 ± 0.17*	−7.19 ± 0.75*	−2.38 ± 0.25*	−0.011 ± 0.006*
Base	91	2	−1.05 ± 0.23*	−1.47 ± 0.17*	−6.95 ± 0.76*	−2.50 ± 0.49*	−0.015 ± 0.006*
Base	91	4	−1.06 ± 0.24*	−1.52 ± 0.19*	−6.98 ± 0.77*	−2.55 ± 0.54*	−0.017 ± 0.006*
Boys	53	1	−1.14 ± 0.29*	−1.05 ± 0.24*	−7.12 ± 0.98*	−2.07 ± 0.63*	−0.001 ± 0.009
Girls	38	1	−0.88 ± 0.41*	−1.94 ± 0.23*	−6.30 ± 1.17*	−3.05 ± 0.69*	−0.028 ± 0.008*
Weeks 1 & 2	34	1	−0.98 ± 0.42*	−1.60 ± 0.24*	−7.71 ± 1.28*	−2.63 ± 0.85*	−0.018 ± 0.010
Weeks 3 & 4	20	1	−1.31 ± 0.55*	−1.10 ± 0.50*	−6.73 ± 1.32*	−2.52 ± 1.27	−0.004 ± 0.019
Weeks 1–4	37	1	−0.92 ± 0.35*	−1.43 ± 0.25*	−5.95 ± 1.17*	−2.31 ± 0.51*	−0.011 ± 0.008
O_3 < 80	91	1	−1.00 ± 0.44*	−0.75 ± 0.29*	−3.05 ± 1.57	−2.09 ± 0.72*	−0.054 ± 0.027*
O_3 < 60	91	1	−1.75 ± 0.40*	−1.19 ± 0.39*	−3.91 ± 1.71*	−1.47 ± 0.97	−0.018 ± 0.033
THI < 78	91	1	−0.96 ± 0.24*	−0.89 ± 0.23*	−7.53 ± 0.95*	−2.46 ± 0.56*	−0.003 ± 0.002
Boys-THI < 78	53	1	−1.03 ± 0.38*	−0.87 ± 0.34*	−7.98 ± 1.10*	−2.15 ± 0.75*	−0.006 ± 0.012
Girls-THI < 78	38	1	−0.86 ± 0.22*	−0.93 ± 0.29*	−6.90 ± 1.70*	−2.90 ± 0.87*	−0.055 ± 0.044

Definition of abbreviations: RD = data from rainy days included in the regressions; THI = temperature-humidity index (heat stress index).

* Significant slope, on average, at $p < 0.05$.

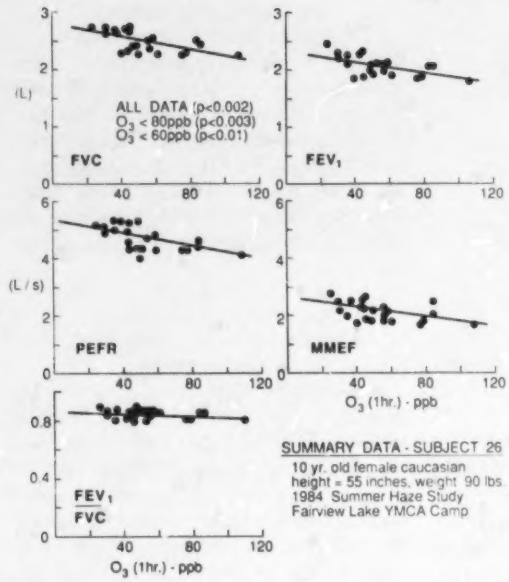
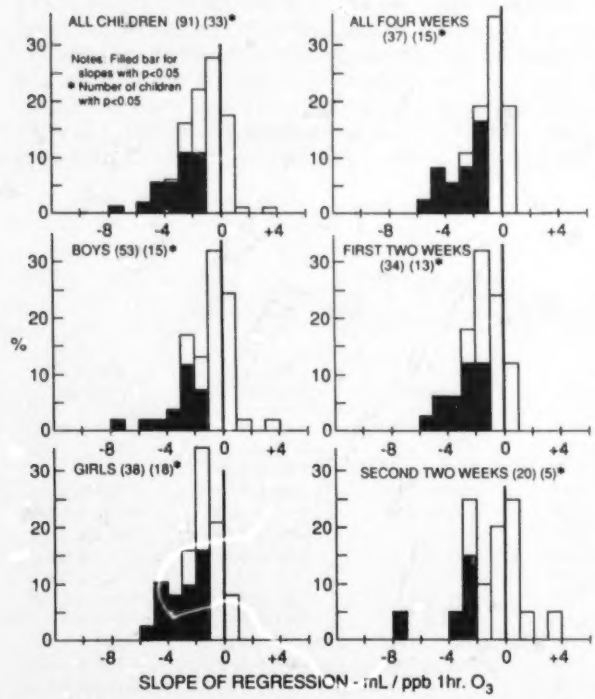


Fig. 2. Plots of function data versus 1-h ozone concentration for one child on 23 study days.

were extended to the 2 and 4 h preceding the function measurements. There were significant group average negative slopes for the regressions for all of the functional indices and all 3 averaging times. Because there were no apparent differences between the mean slopes or their variability within the group with 1-, 2-, and 4-h averaging times, further analyses of variation within subsets were limited to the 1-h averaging time. The data and regression lines for the 1-h averaging time for one child, a 10-yr-old girl, are shown in figure 2. For FVC, PEFR, and FEF_{25-75} there were no significant differences between the slopes for girls and boys, or between the slopes for the groups studied in the first 2 wk, the second 2 wk, or all 4 wk. For FEV_1, the girls had regression slopes almost twice as large as those of the boys.

To explore whether there was an O_3 threshold for decrements in function, regressions were also run with data sets truncated at 80 and 60 ppb O_3. The variability in slope was increased substantially in all cases for the truncated data sets, as would be expected when a key variable covers a narrower range, but the average slopes remained negative in all cases, suggesting that the thresholds, if they exist, were below 60 ppb. The only significant changes in slopes were for PEFR, where the slopes were about half of those determined with the full data sets.

Histograms of the FEV_1, and PEFR slopes are shown in figures 3 and 4. For FEV_1, 33 (15 boys and 18 girls) of the 91 children had slopes that were significantly different from zero based on $p < 0.05$ (two-tailed), and all 33 were negative. For PEFR, 37 (22 boys and 15 girls) of the 91 children had slopes significantly different from zero, with 35 of them negative. The distributions of the slopes for


ALL CHILDREN (91) (33)*
Notes: Filled bar for slopes with p<0.05
* Number of children with p<0.05
ALL FOUR WEEKS (37) (15)*
BOYS (53) (15)*
FIRST TWO WEEKS (34) (13)*
GIRLS (38) (18)*
SECOND TWO WEEKS (20) (5)*
%
SLOPE OF REGRESSION - mL / ppb 1hr. O3

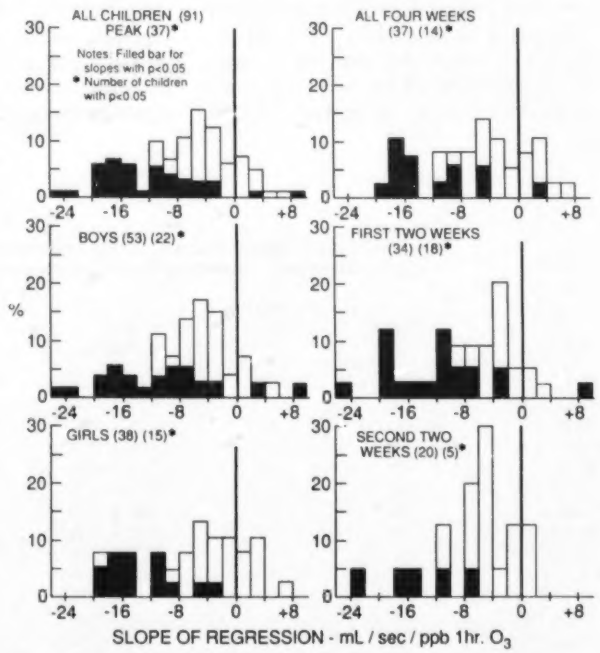

ALL CHILDREN (91) PEAK (37)*
Notes: Filled bar for slopes with p<0.05
* Number of children with p<0.05
ALL FOUR WEEKS (37) (14)*
BOYS (53) (22)*
FIRST TWO WEEKS (34) (18)*
GIRLS (38) (15)*
SECOND TWO WEEKS (20) (5)*
%
SLOPE OF REGRESSION - mL / sec / ppb 1hr. O3

Fig. 3 (*left*). Histograms of regression slopes for FEV_1, versus 1-h ozone concentration. The numbers of children in each group are indicated in parentheses.

Fig. 4 (*right*). Histograms of regression slopes for PEFR versus 1-h ozone concentration.

FEV_1 and PEFR for the boys and girls separately and for the children in each camp period appear to be similar to the distributions for all of the children together.

Stepwise Multiple Regressions

The results of the stepwise multiple regression selection among the 7 environmental variables showed that for FEV_1 the 1-h O_3 concentration was selected in 33 of the 91 children, and had a negative slope in 28 of them. The only other variables having more cases of negative than positive slopes for FEV_1 were daily cumulative O_3 exposure (23 of 31) and ambient temperature (28 of 45). For PEFR, the 1-h O_3 concentration was selected in 44 children, and had a negative slope in 34 of 44. The only other variable having more cases of negative than positive slopes for PEFR was relative humidity (26 of 40).

On the basis of the results of the stepwise multiple regression using 7 variables, we selected 1-h O_3 concentration, cumulative daily O_3 exposure, and a simple composite heat stress index (THI) as the variables for further analyses. The THI combines temperature and humidity according to a formula used by the U.S. Weather Bureau, i.e., THI (°F) = (dry bulb + wet bulb) 0.4 + 15.

Analysis of Residuals from 1-h Ozone versus Function Regressions

Further exploratory analyses were performed by calculating the average of the deviations (residuals) from the 1-h O_3 versus the measured functions (i.e., FVC, FEV_1, PEFR, FEF_{25-75}, and FEV_1/FVC) for each child for each exposure variable. This was done for each of the following exposure variables: number of hours between 9 A.M. and function measurement, cumulative daily O_3 exposure from 9 A.M. until the hour of function measurement, average H^+ exposure during day of function measurement, average PM_{15} exposure during day of measurement, ambient temperature during the hour preceding the function measurement, ambient relative humidity during the hour preceding the function measurement, and THI.

There was no systematic effect of cumulative daily O_3 exposure apparent from these analyses, but there was an increased variability in the functional indices for cumulative exposures larger than about 500 ppb-hours. This is illustrated in figure 5 for FVC, FEV_1, and PEFR. The variability for FEF_{25-75} was very similar to that shown for PEFR.

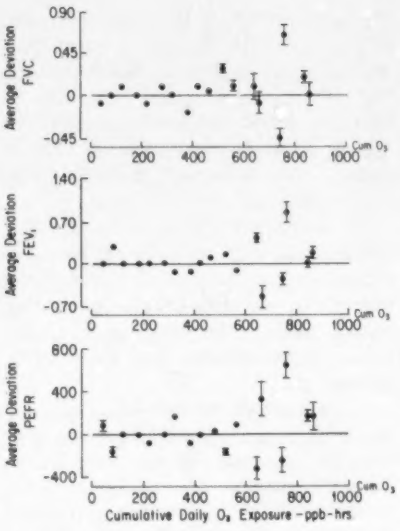


Fig. 5. Average deviations from linear regressions between function and 1-h ozone concentration as a function of cumulative daily ozone exposure in ppb-hours after 9 A.M. Panel A is for FVC; Panel B for FEV_1, and Panel C for PEFR.

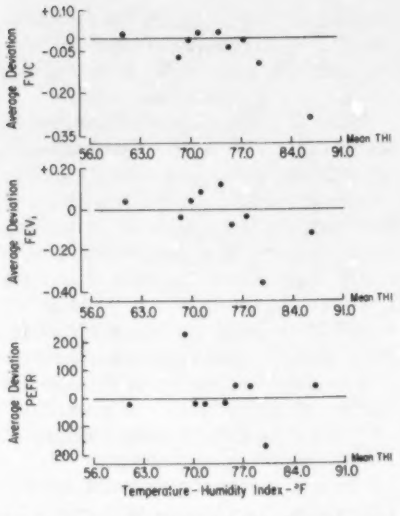


Fig. 6. Average deviations from linear regressions between function and 1-h ozone concentration as a function of the temperature-humidity index in ° F. The Panel A is for FVC; Panel B for FEV_1, and Panel C for PEFR.

The only exposure variable that showed consistent deviations from the regressions of 1-h O_3 versus function was THI. The deviations for FVC and FEV_1 were not proportional to THI, but became important for THI > 78°F, as illustrated in figure 6. There was no apparent threshold for the deviations for PEFR or FEF_{25-75}. The influence of the elevated thermal stress on respiratory function was explored by recalculating the coefficients for data sets truncated by the removal of data collected at THI > 78°F. The results are shown at the bottom of table 1. The revised regression slopes were essentially the same for FVC, PEFR, and FEF_{25-75}. On the other hand, the slopes for all children for FEV_1 and the FEV_1/FVC ratio were significantly reduced, and the differences between girls and boys in FEV_1 slope were greatly reduced.

Discussion

The variability of the individual slopes can be attributed in major part to 2 factors. One is the variability in the responsiveness of the individual children to the effects of ambient ozone. The other is the inherent variability of repeated function measurements. The variability in responsiveness in this study could, in turn, be attributed to variations in inherent sensitivity to a given O_3 challenge, and to variations in ventilation rates among the children. McDonnell and coworkers (13), in chamber studies in adults involving replicate exposures in the same individuals separated by intervals of 3 wk to 10 months, showed that sensitivity was both reproducible in individuals and highly variable among the population. There was almost certainly more variation in ventilation rate among the children in the camp study than among the adults in the chamber study where they all performed the same exercise. Children's activity levels, even when they are engaged in programmed group activities, would be considerably more variable from child to child and day to day.

The inherent variability of repeated function measurements is of sufficient magnitude to partially or completely obscure the effects of the O_3 exposures received by most of the children in this study, especially among those who are less responsive. As expected, the frequency of statistically significant slopes was lower among children who spent only 2 wk at camp in comparison with children who were at camp for 4 wk and were measured on approximately twice as many days. For example, 41% of the 4-wk children had statistically significant negative slopes for FEV_1, whereas the corresponding percentage for the 2-wk children was 33%.

Considering the inherent variability of repeated function measurements, and the expected presence of relatively insensitive individuals among the population, the finding of a small percentage of positive slopes is not surprising. None of the

positive slopes were significant for FEV_1. For PEFR, an inherently more variable measurement than FEV_1, only 2 of the 37 significant slopes were positive.

Taken as a whole, the distributions of slopes support an association of ambient O_3 with decreased lung function in the population. However, it is important to note that the magnitude of each slope is an estimate with a considerable uncertainty and cannot provide a precise predictor for the effects to be expected in any given child. On the other hand, the population mean responses can provide unbiased estimates of the average impact of ambient O_3 on respiratory function in healthy children engaged in normal recreational activities.

The analyses of the pulmonary function versus 1-h O_3 data sets truncated at 80 and 60 ppb O_3 (table 1) demonstrate that O_3 is strongly associated with decrements in spirometric indices extending down into the ambient concentration range encountered in clean background air. The data also indicate that it is reasonable to describe the O_3 exposure-response relationships by linear functions, at least for concentrations up to the current NAAQS, for FVC, FEV_1, and FEF_{25-75}. For PEFR, there was a suggestion of a greater rate of change in function for $O_3 > 80$ ppb. The data of McDonnell and colleagues (14) on adults appear to show an increasing rate of change in all measured functions for O_3 concentrations above 180 ppb.

For the purpose of the discussion that follows, the responses are expressed in terms of volume or flow rate changes per ppb of O_3, including the results of laboratory studies comparing a single exposure concentration and clean background air.

A summary of the regression slopes between O_3 concentration and respiratory function indices in this and other studies on children is shown in table 2. It can be seen that the results of this study are highly consistent with the others, at least in terms of showing O_3-associated decrements in function in active children. The magnitudes of the coefficients in this study are closest to those of our earlier study in Indiana, PA, in which the exposures and activity levels were the most similar. As expected, the coefficients were substantially higher than those from Mendham, NJ, where the children's activity levels, by our own observations, were lower than those we observed in the studies in Indiana and Fairview Lake. The average regression slopes in this study were not significantly affected by the inclusion of data from 1 full and 2 partial days of rain with reduced levels of physical activity.

Comparisons between the results of our studies and those performed in Chapel Hill (5), Los Angeles (6, 7), and Seattle (15) must be made with caution, since the latter groups all involved step-function exposures within chambers. The exposures lasted 1 h in Los Angeles and Seattle, and 2.5 h in Chapel Hill, with clean air exposures preceding and following the O_3 exposure. Another factor that may account for differences between the results in this study and those from the chamber exposures in Chapel Hill and Seattle is that the chamber exposures were to O_3 alone. The Los Angeles group was exposed to O_3 within an ambient pollutant mixture and, in this respect, had more comparable exposures to those of the children in the camp studies.

A number of controlled chamber ex-

TABLE 2

EFFECT OF OZONE ON SPIROMETRIC INDICES IN HEALTHY CHILDREN

Study Location	Children (*n*)	Age Range (*yr*)	Physical Activity Level	Maximal 1-h O_3 Concentration (*ppb*)	Average Regression Slopes—Function vs. O_3 Conc. FVC (*ml/ppb*)	FEV_1 (*ml/ppb*)	PEFR (*ml/s/ppb*)	FEF_{25-75} (*ml/s/ppb*)	Remarks	References
Indiana, PA									YMCA summer day	(1)
Total	58	8–13	Moderate	110	−1.06	−0.78	—	—	camp—2 wk;	
Boys	24				−0.76	−0.41	—	—	continuous exposure	
Girls	34				−1.27	−1.04	—	—	to ambient air	
Mendham, NJ									Private summer	(2)
Total	39	7–13	Low	185	−0.12	−0.28	−2.99	−0.55	day camp—5 wk;	(3)
Boys	17				+0.06	−0.11	−1.74	−0.38	continuous exposure	
Girls	22				−0.29	−0.42	−3.95	−0.68	to ambient air	
Chapel Hill, NC									2.5 h sham and	
Boys	23	8–11	Very High	120	−0.33	−0.47	−1.83	−0.58	120 ppb chamber exposures with intermittent exercise at 39 l/min.	(5)
Los Angeles, CA									1-h purified air	(6, 7)
Total	59	12–15	High	150	−0.72	−0.80	−1.57	−0.72	and 150-ppb	
Boys	46				—	−0.73	—	—	O_3 in ambient air	
Girls	13				—	−1.27	—	—	in chamber, with continuous exercise at 32 L/min	
Seattle, WA									1 h sham and 120	(15)
Total	10	13–18	At rest	120	—	0	—	—	ppb O_3 chamber	
Boys	4	13–18			—	—	—	—	exposures at	
Girls	6	13			—	—	—	—	rest	
Fairview Lake, NJ									YMCA summer camp—	
Total	91	7–13	Moderate	113	−1.03	−1.42	−6.78	−2.48	children in residence	
Boys	53				−1.14	−1.05	−7.12	−2.07	for 2 or 4 wk;	
Girls	38				−0.88	−1.94	−6.30	−3.05	continuous exposure to ambient air	

posure studies have demonstrated that activity level is as important a determinant in functional responsiveness to O_3 exposure as the concentration of O_3. These data have recently been summarized by Hazucha (16). Thus, the lack of any effect for the Seattle group, who were exposed at rest, and the greater effects in our own studies in Indiana and Fairview Lake in comparison to our study in Mendham are in line with expectations. On the other hand, the Los Angeles population (12 to 15 yr of age, mean ventilation = 32 L/min) and the Chapel Hill population (8 to 11 yr of age, mean ventilation = 39 L/min during exercise) were both at greater activity levels than the camp children, and might be expected to have had larger coefficients. The 2.5-h exposure in Chapel Hill included 1 h of exercise, whereas the Los Angeles group was exposed for 1 h with continuous exercise. Thus, if time of exposure while exercising is a critical exposure parameter, the effective exposure times were reasonably similar. Because the Chapel Hill children had a greater activity level than did the Los Angeles group and were smaller, they should have had greater rather than lesser coefficients because of the greater relative level of activity. These considerations suggest that other constituents in the ambient pollutant mixture potentiate the O_3 response. However, in another study in Los Angeles on adult cyclists in the same chamber, Avol and associates (17) found O_3 in ambient air had the same effect on FVC and FEV_1 as did O_3 alone added to purified air at the same concentration.

FEV_1 was affected more than the other spirometric indices by the truncation of the data set at THI > 78° F in the linear regressions of 1-h O_3 and function (table 1). Truncation of THI > 78° F had an even greater effect on the FEV_1/FVC ratio, suggesting that heat stress had more effect on the resistive component of FEV_1 than on the component attributable to volumetric changes. There were no comparable changes in PEFR or FEF_{25-75}, which should also be affected by changes in flow resistance.

The reduced FEV_1 slopes for the data sets restricted to THI < 78° F were due, almost entirely, to a reduction (by half) of the average slope for the girls. It is not clear why the elimination of data involving heat stress should change FEV_1 but not the other indices in girls, or why it had little, if any, effect on the results for boys.

Unfortunately, the results of this study add little additional information to our understanding of the effects of other air constituents on responses to O_3. We specifically examined the influence of aerosol H^+ and PM_{15} concentrations on the O_3 response, and could not find any association at the moderate exposure concentrations experienced at this site during the summer of 1984.

The generally larger coefficients from the camp studies than those from the chamber studies could be interpreted as indicating that both cumulative O_3 exposure and THI affect the responses. If the O_3 concentration in the hour preceding the spirometry was the sole factor affecting the response, then the variability of the coefficients should increase with larger averaging times. The results in table 1 do not show this to be the case, suggesting that the use of a longer averaging time introduces another, counterbalancing factor. The analysis of residuals as a function of daily cumulative O_3 exposure, as illustrated in figure 5, did not show any consistent trends with increasing exposure. They did, however, show greater variability of the residuals for O_3 exposures > 500 ppb-hours than for lower values. As indicated by the error bars in figure 5, some of the greater variability was due to the smaller numbers of observations at the higher cumulative exposures. A possible factor for the remaining variability could be the stimulation of adaptive responses by larger cumulative exposures.

In almost every case where data have been collected on both boys and girls, the average responses of the girls have been greater. The observed differences between the coefficients for boys and girls may be due to differences in level of physical activity rather than to intrinsic sensitivity. In our earlier study in Indiana, PA, we found that differences in overall coefficients disappeared when the analysis was restricted to day-pairs of comparable activity (1). In this study, the biggest difference in coefficient was for FEV_1, where the girls had a coefficient almost twice as large as that for the boys. When the comparison was restricted to the 15 boys and 18 girls with individually significant regression slopes, the mean slopes were almost the same. Furthermore, when the comparison was made for the data set with THI < 78° F, the average coefficients for the boys and girls were also almost the same. This suggests that girls are more affected by heat stress than the boys. If there are really sex-based differences, the reasons are unknown, and could best be explored further in controlled laboratory studies.

The health significance of the responses found in this study are difficult to evaluate. There was no evidence of respiratory morbidity in this study, and this was consistent with the work of others. Both Avol and associates (7) and McDonnell and coworkers (5, 18) have reported that children have similar functional responses to O_3 as adults, but without the symptomatic responses seen in adults.

In terms of the functional changes, the average responses are relatively small. For example, the average coefficient for FEV_1 was −1.42 ml/ppb, which translates into a reduction of 170 ml at the NAAQS or ∼7.7%. If one considers the average response for the 33 children (36%) with individually significant FEV_1 responses, the coefficient was −2.97 ml/ppb, leading to a 356 ml (∼ 16%) loss at the NAAQS. If one considers the upper decile of response, the coefficient is increased to ∼ 3.5 ml/ppb or 420 ml (∼ 19%) at the NAAQS. The corresponding values for mean change and upper decile responses at the NAAQS for FVC were 124 and 365 ml (4.9 and 14%), for PEFR 814 and 2,040 ml/s (∼ 17 and 42%), and for FEF_{25-75} were 298 and 880 ml/s (11 and 33%). If a population mean response of 10% decrement in function were used as a benchmark for adverse effects, then the current NAAQS would have very little margin of safety for FVC and FEV_1, and would not protect against excessive decrements in PEFR and FEF_{25-75}.

An examination of the results summarized in figures 3 and 4 suggests that the population mean changes are largely driven by the changes occurring in a subset of the population. For FEV_1, the mean response of the 33 children with individually significant slopes was −2.97 ml/ppb. If this response was subtracted from that for the whole group of 91 children, the average response for the other 58 children was only −0.54 ml/ppb. For PEFR, the mean response of the 37 children with individually significant slopes was −12.09 ml/s/ppb, and the average response of the other 54 children was −3.15 ml/s/ppb. Interindividual variations in responses to O_3 exposure have been observed in the controlled exposures in chambers (5–7, 13, 14, 16–18), but the reasons for such variations are not known.

If, as discussed previously, cumulative daily exposure accounts for the larger coefficients reported for this study in

comparison with chamber exposure studies, then the current NAAQS may have an inappropriate averaging time. Rombout and coworkers (19) have recently proposed a rationale for an 8-h O_3 standard on the basis of the cumulative effects seen in animal studies, and the observations that O_3 concentrations in the eastern United States and western Europe sometimes have prolonged afternoon maxima with 8-h concentrations above 90% of the 1-h maximum. Thus, a NAAQS with a 1-h averaging time may protect against excessive changes in function when the O_3 exposure occurs as a sharp daily peak, but fail to protect when there is a broad peak with the same peak concentration. More data are needed on the cumulative effects of O_3 in order to properly address this important issue.

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